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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/977,831	BONNY, CHRISTOPHE	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14 and 45-54* is/are pending in the application.

4a) Of the above claim(s) *45 and 50-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14, 46-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed on 1/30/04 has been considered. The amendment cancels 1-13, amends claim 14 and adds new claims 36-54.

2. In response to the non-responsive amendment mailed on 4/28/04, applicants amend claims 14, 50, 52-53, and cancels claims 15-44.

3. Applicants' amendments filed on 5/28/04 has been fully considered and entered into the application.

4. Claims 14, 45-54 are currently pending in this application.

5. Newly submitted claims 50-54 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The originally elected method is drawn to a method of translocating a transporter peptide into a pancreatic beta cell, and the newly added claim recites further method steps of detecting the presence of transporter peptide. The newly added claims are distinct from the originally elected and examined method. The method of translocating a transporter peptide does not require the method steps of method of detecting the presence of transporter peptide inside the cell; both the methods have different utilities, i.e., the method of detection of the presence of transporter peptide inside a cell is useful in *in-vitro or in in-vivo* diagnostic assay and the method of translocating the transporter peptide into a cell is useful in therapy.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 50-54 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

6. Claim 45 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/15/03.

NOTE applicants have elected SEQ ID NO: 1 as the species of transporter peptide on 7/15/03, and the newly added claim is drawn to 'retro-inverso' peptide, which has a different sequence from the elected sequence of SEQ ID NO; 1. Thus the instant claim 45 is withdrawn from consideration.

7. Claims 14, 46-49 are currently being examined in this application.

8. Applicants' amendment to the specification regarding the priority to the provisional application 60/240,315 has been noted.

9. The information disclosure statement filed on 1/30/04 has been fully considered and entered into the application.

10. The objection to claim 14, set forth in the previous office action has been withdrawn in view of the amendment to the claim.

11. In view of the amendments filed to claim 14, the lack of written description rejection and the incomplete claim rejection of record have been withdrawn.

New Claim Rejections Necessitated by the Amendment

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

13. Claims 48-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claims 48-49 recite the limitation "the cells". There is insufficient antecedent basis for this limitation in the claims or in claim 14.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

16. Claims 14, 46-48 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 93/18759 (Smith et al).

The instant independent claim recites 'a method of translocating a transporter peptide into a pancreatic B-cell, comprising contacting the pancreatic B-cell with a transporter peptide for a time and under conditions sufficient to allow a transporter peptide to translocate across the membrane of B-cell, wherein the transporter peptide comprises the amino acid sequence of SEQ ID NO:1.'

Note the transporter peptide of the instant claim is considered as the transporter peptide, which has the sequence of SEQ ID NO: 1 (Arg-Arg-Thr-Lys) and additional sequences.

WO 93/18759 (Smith et al) teaches a DNA transporter system and method of use. The reference teaches that the DNA transporter system comprises a first binding molecule covalently linked to a surface ligand; a second DNA binding molecule and a nuclear ligand (i.e., see page 2, in the 'summary of Invention and claim 1). The reference teaches that the nuclear ligand is capable of recognizing and transporting the transporter system through a nuclear membrane (i.e., see page 2) (refers to the instant claim translocating the transporter peptide across the membrane of the cell). The reference teaches peptide ligands used in the claimed invention (i.e., see figure 18). The Peptide 8 of the reference (i.e., see figure 18 and claim 20) is 12 amino acids long and read on the instant claim transporter peptide comprising the sequence of SEQ ID NO: 1 (Arg-Arg-Thr-Lys). The reference teaches a transporter system comprising a compound CXLIj (i.e., see claim 62, or figure 17), in which 'z' is the transporter peptide, which is peptide 8. The reference teaches that the transporter system transports DNA into cells, *in vivo* and *in vitro* targeting of the insertion of DNA into specific cells, prevention and treatment of

disease. The reference teaches insulin-like growth factor I receptor as the surface ligand used in the reference transporter system (i.e., see page 3). The insulin-like growth factor receptor is present on the pancreatic beta cells. Thus the transporter system of the reference with insulin like growth factor I receptor as the surface ligand is specific to the pancreatic cells. The reference claim 43 recites a method of introducing DNA into a cell comprising contacting the cell with the transporter system of claim 1 (refers to instant claim method). The reference clearly anticipates the claimed invention.

17. Claims 14, 46-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Woo et al (US patent 5,994,109).

The instant independent claim recites 'a method of translocating a transporter peptide into a pancreatic B-cell, comprising contacting the pancreatic B-cell with a transporter peptide for a time and under conditions sufficient to allow a transporter peptide to translocate across the membrane of B-cell, wherein the transporter peptide comprises the amino acid sequence of SEQ ID NO:1.'

Note the transporter peptide of the instant claim is considered as the transporter peptide, which has the sequence of SEQ ID NO: 1 (Arg-Arg-Thr-Lys) with additional sequences and/or components.

Woo et al teach a DNA transporter system and method of use. The reference teaches that the DNA transporter system comprising a binding complex. The binding complex comprising a binding molecule covalently linked to a surface ligand, a nuclear ligand (i.e., see abstract). The reference teaches that the 'nucleic acid transporter system' used herein refers to a molecular complex which is capable of efficiently transporting nucleic acid through the cell membrane (i.e., see column 4). The reference teaches that

the nuclear ligand is capable of recognizing and transporting the transporter system through a nuclear membrane (i.e., see column 8) (refers to the instant claim translocating the transporter peptide across the membrane of the cell). The reference teaches peptide ligands used in the claimed invention (i.e., see figure 18 and column 8). The Peptide 8 of the reference (i.e., see figure 18) is 12 amino acids long and read on the instant claim transporter peptide comprising the sequence of SEQ ID NO: 1 (Arg-Arg-Thr-Lys). The reference teaches a transporter system comprising a compound CXLIj (i.e., see figure 17B), in which 'z' is the transporter peptide, which is peptide 8 linked to a chemical group. The reference teaches that the transporter system transports DNA into cells, *in vivo* and *in vitro* targeting of the insertion of DNA into specific cells, prevention and treatment of disease. The reference teaches insulin-like growth factor I receptor as the surface ligand used in the reference transporter system (i.e., see column 7). The insulin-like growth factor receptor is present on the pancreatic beta cells. Thus the transporter system of the reference with insulin like growth factor I receptor as the surface ligand is specific to the pancreatic cells. The reference claims recite a method of introducing DNA into a cell comprising contacting the cell with the transporter system (refers to instant claim method). The reference teaches methods of administration of the reference transporter system into body (i.e., see columns 47-48). The reference clearly anticipates the claimed invention.

18. Claims 14, 46-49 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2003/0104622 A1 (Robbins et al).

The instant independent claim recites 'a method of translocating a transporter

peptide into a pancreatic B-cell, comprising contacting the pancreatic B-cell with a transporter peptide for a time and under conditions sufficient to allow a transporter peptide to translocate across the membrane of B-cell, wherein the transporter peptide comprises the amino acid sequence of SEQ ID NO:1.'

Note the transporter peptide of the instant claim is considered as the transporter peptide, which has the sequence of SEQ ID NO: 1 (Arg-Arg-Thr-Lys) with additional sequences and/or components.

Robbins et al teach internalizing peptides, which facilitate the uptake and transport of cargo into the cytoplasm and nuclei of cells both *in vivo* and *in vitro* (i.e., see the abstract). The reference teaches internalizing peptide of the invention may have the amino acid sequence G**RRTK**KQRRQKKPP (SEQ ID NO: 75) (refers to the transporter peptide of the instant claims). The reference teaches that the complex comprising an internalizing peptide linked to cargo with target cells and measuring the efficiency of transfer of the peptide-cargo complex to the target cells; and the reference teaches that the inventions useful to delivery of cargo into cells in vivo and can facilitate in situ or localized delivery of cargo in vivo (refers to the instant claimed method). The reference teaches that the internalizing peptides of the invention can be used to deliver inhibitors of NF-kB to isolated β cells (refers to the pancreatic B cells of the instant claims). The reference teaches administration of internalizing peptide cargo in vivo by oral, pulmonary, parenteral, inhalation, transdermal, nasal routes of administration (i.e., see page 15, 0156). The reference teaches that the internalizing peptide is administered with a carrier, such as saline or buffered saline, which would read on the pharmaceutical

composition of the transporter peptide of the instant claims. The reference clearly anticipates the claimed invention.

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. Claims 14, 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/18759 and Pub No.US 2003/0104622 A1 (Robbins et al, effective filing date September 01, 1999).

The instant independent claim recites 'a method of translocating a transporter peptide into a pancreatic B-cell, comprising contacting the pancreatic B-cell with a transporter peptide for a time and under conditions sufficient to allow a transporter peptide to translocate across the membrane of B-cell, wherein the transporter peptide comprises the amino acid sequence of SEQ ID NO:1.'

Note the transporter peptide of the instant claim is considered as the transporter peptide, which has the sequence of SEQ ID NO: 1 (Arg-Arg-Thr-Lys) with additional sequences and/or components.

WO 93/18759 (Smith et al) teaches a DNA transporter system and method of use. The reference teaches that the DNA transporter system comprises a first binding molecule covalently linked to a surface ligand; a second DNA binding molecule and a nuclear ligand (i.e., see page 2, in the 'summary of Invention and claim 1). The reference teaches that the nuclear ligand is capable of recognizing and transporting the transporter system through a nuclear membrane (i.e., see page 2) (refers to the instant claim

translocating the transporter peptide across the membrane of the cell). The reference teaches peptide ligands used in the claimed invention (i.e., see figure 18). The Peptide 8 of the reference (i.e., see figure 18 and claim 20) is 12 amino acids long and read on the instant claim transporter peptide comprising the sequence of SEQ ID NO: 1 (Arg-Arg-Thr-Lys). The reference teaches a transporter system comprising the compound CXLlj (i.e., see claim 62, or figure 17), in which 'z' is the transporter peptide, which is peptide 8. The reference teaches that the transporter system transports DNA into cells, *in vivo* and *in vitro* targeting of the insertion of DNA into specific cells, prevention and treatment of disease. The reference teaches insulin-like growth factor I receptor as the surface ligand used in the reference transporter system (i.e., see page 3). The insulin-like growth factor receptor is present on the pancreatic beta cells. Thus the transporter system of the reference with insulin like growth factor I receptor as the surface ligand is specific to the pancreatic cells. The reference claim 43 recites a method of introducing DNA into a cell comprising contacting the cell with the transporter system of claim 1 (refers to instant claim method).

The claimed invention differs from the prior art teachings by reciting 'pharmaceutically acceptable salt of the transporter peptide.' Smith et al teach DNA transporter system comprising a nuclear ligand, which is capable of recognizing and transporting the transporter system through a nuclear membrane. The reference teaches the peptides used as nuclear ligands in the DNA transporter system. The reference peptide 8 reads on the instant claimed transporter peptide. Smith et al teach that the transporter system transports DNA into cells, *in vivo* and *in vitro* targeting of the insertion of DNA into specific cells, prevention and treatment of disease. Smith et al do

not reach a pharmaceutically acceptable salt of the transporter peptide. However, Robbins et al teach internalizing peptides, which facilitate the uptake and transport of cargo into the cytoplasm and nuclei of cells both *in vivo* and *in vitro* (i.e., see the abstract). The reference teaches internalizing peptide of the invention may have the amino acid sequence G**RRTK**KQRRQKKPP (SEQ ID NO: 75) (refers to the transporter peptide of the instant claims). The reference teaches that the complex comprising an internalizing peptide linked to cargo with target cells and measuring the efficiency of transfer of the peptide-cargo complex to the target cells; and the reference teaches that the inventions useful to delivery of cargo into cells in vivo and can facilitate in situ or localized delivery of cargo in vivo (refers to the instant claimed method). The reference teaches that the internalizing peptides of the invention can be used to deliver inhibitors of NF-kB to isolated β cells (refers to the pancreatic B cells of the instant claims). The reference teaches administration of internalizing peptide cargo in vivo by oral, pulmonary, parenteral, inhalation, transdermal, nasal routes of administration (i.e., see page 15, 0156). The reference teaches that the internalizing peptide is administered with a carrier, such as saline or buffered saline, which would read on the pharmaceutical composition of the transporter peptide of the instant claims. Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the DNA transporter system taught by Smith et al to prepare a pharmaceutical composition and such that the transporter system is used in treatment of diseases. A person skilled in the art would have been motivate to use prepare pharmaceutical compositions of the DNA transporter system taught by the reference such the compounds are useful in therapy.

20. Claims 14, 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,994,109 (Woo et al).

The instant independent claim recites 'a method of translocating a transporter peptide into a pancreatic B-cell, comprising contacting the pancreatic B-cell with a transporter peptide for a time and under conditions sufficient to allow a transporter peptide to translocate across the membrane of B-cell, wherein the transporter peptide comprises the amino acid sequence of SEQ ID NO:1.'

Note the transporter peptide of the instant claim is considered as the transporter peptide, which has the sequence of SEQ ID NO: 1 (Arg-Arg-Thr-Lys) with additional sequences and/or components.

Woo et al teach a DNA transporter system and method of use. The reference teaches that the DNA transporter system comprising a binding complex. The binding complex comprising a binding molecule covalently linked to a surface ligand, a nuclear ligand (i.e., see abstract). The reference teaches that the 'nucleic acid transporter system' used herein refers to a molecular complex which is capable of efficiently transporting nucleic acid through the cell membrane (i.e., see column 4). The reference teaches that the nuclear ligand is capable of recognizing and transporting the transporter system through a nuclear membrane (i.e., see column 8) (refers to the instant claim translocating the transporter peptide across the membrane of the cell). The reference teaches peptide ligands used in the claimed invention (i.e., see figure 18 and column 8). The Peptide 8 of the reference (i.e., see figure 18) is 12 amino acids long and read on the instant claim transporter peptide comprising the sequence of SEQ ID NO: 1 (Arg-Arg-Thr-Lys). The reference teaches a transporter system comprising a compound CXLIj (i.e., see figure

17B), in which 'z' is the transporter peptide, which is peptide 8 linked to a chemical group. The reference teaches that the transporter system transports DNA into cells, *in vivo* and *in vitro* targeting of the insertion of DNA into specific cells, prevention and treatment of disease. The reference teaches insulin-like growth factor I receptor as the surface ligand used in the reference transporter system (i.e., see column 7). The insulin-like growth factor receptor is present on the pancreatic beta cells. Thus the transporter system of the reference with insulin like growth factor I receptor as the surface ligand is specific to the pancreatic cells. The reference claims recite a method of introducing DNA into a cell comprising contacting the cell with the transporter system (refers to instant claim method). The reference teaches methods of administration of the reference transporter system into body (i.e., see columns 47-48). The reference teaches methods of treating cardiovascular disease using the nucleic acid transporter system (i.e., see column 86).

The claimed invention differs from the prior art teachings by reciting 'pharmaceutically acceptable salt of the transporter peptide.' Woo et al teach DNA transporter system comprising a nuclear ligand, which is capable of recognizing and transporting the transporter system through a nuclear membrane. The reference teaches the peptides used as nuclear ligands in the DNA transporter system. The reference peptide 8 reads on the instant claimed transporter peptide. Woo et al teach that the transporter system transports DNA into cells, *in vivo* and *in vitro* targeting of the insertion of DNA into specific cells, prevention and treatment of disease.). The reference teaches methods of administration of the reference transporter system into body. The reference teaches methods of treating cardiovascular disease using the nucleic

acid transporter system. Woo et al do not reach a pharmaceutically acceptable salt of the transporter peptide. However, it would have been obvious to one skilled in the art at the time the invention was made to prepare pharmaceutically acceptable salt of the transporter peptide such that it is used in treatment of diseases.

Response to Arguments

21. Applicant's arguments with respect to claim 14 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

22. No claims are allowed.

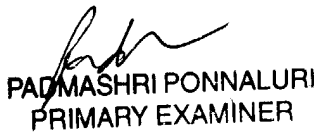
23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

17 August 2004